

## PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents  
 United States Patent and Trademark  
 Office  
 Box PCT  
 Washington, D.C.20231  
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 26 September 2000 (26.09.00)	
International application No. PCT/US99/26746	Applicant's or agent's file reference P32185
International filing date (day/month/year) 12 November 1999 (12.11.99)	Priority date (day/month/year) 12 November 1998 (12.11.98)
Applicant BENINCOSA, Lisa et al	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

09 May 2000 (09.05.00)

in a notice effecting later election filed with the International Bureau on:

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Cormettes 1211 Genève 20, Switzerland	Authorized officer S. Mafia
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

REC'D 15 MAY 2001

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70) 14

Applicant's or agent's file reference P32185	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/26746	International filing date (day/month/year) 12 NOVEMBER 1999	Priority date (day/month/year) 12 NOVEMBER 1998
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 31/44, 31/425 and US Cl.: 514/275, 252, 369, 337		
Applicant SMITHKLINE BEECHAM CORPORATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets.

This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I  Basis of the report
- II  Priority
- III  Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV  Lack of unity of invention
- V  Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI  Certain documents cited
- VII  Certain defects in the international application
- VIII  Certain observations on the international application

Date of submission of the demand 09 MAY 2000	Date of completion of this report 07 APRIL 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer  SHEP ROSE
Faxsimile No. (703) 305-3230	Telephone No. (703) 308-1235

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/26746

## I. Basis of the report

## 1. With regard to the elements of the international application:\*

 the international application as originally filed the description:

pages 1-13

pages NONE

pages NONE

, as originally filed  
, filed with the demand  
, filed with the letter of the claims:

pages 14-16

pages NONE

pages NONE

pages NONE

, as originally filed  
, as amended (together with any statement) under Article 19  
, filed with the demand  
, filed with the letter of the drawings:

pages 1-2

pages NONE

pages NONE

, as originally filed  
, filed with the demand  
, filed with the letter of the sequence listing part of the description:

pages NONE

pages NONE

pages NONE

, as originally filed  
, filed with the demand  
, filed with the letter of

## 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

 the language of a translation furnished for the purposes of international search (under Rule 23.1(b)). the language of publication of the international application (under Rule 48.3(b)). the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

 contained in the international application in printed form. filed together with the international application in computer readable form. furnished subsequently to this Authority in written form. furnished subsequently to this Authority in computer readable form. The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished. The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4.  The amendments have resulted in the cancellation of: the description, pages NONE the claims, Nos. NONE the drawings, sheets ~~fig~~ NONE5.  This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

the entire international application.

claims Nos. 4-11, 13-15, 17, 20, 21

because:

the said international application, or the said claim Nos.   relate to the following subject matter which does not require international preliminary examination (*specify*).

the description, claims or drawings (*indicate particular elements below*) or said claims Nos.   are so unclear that no meaningful opinion could be formed (*specify*).

the claims, or said claims Nos. (See Attached) are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for said claims Nos.  .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

the written form has not been furnished or does not comply with the standard.

the computer readable form has not been furnished or does not comply with the standard.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/26746

**V. Reas ned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. statement**

Novelty (N)	Claims <u>1-3, 12, 18-19</u>	YES
	Claims <u>16, 17</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-3, 12, 16-19</u>	NO
Industrial Applicability (IA)	Claims <u>1-3, 12, 16-19</u>	YES
	Claims <u>NONE</u>	NO

**2. citations and explanations (Rule 70.7)**

(See Supplemental Sheet.)

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**III. NON-ESTABLISHMENT OF REPORT:**

Claim numbers 4-11, 13-15, 17, 20, 21 are so inadequately supported by the description that no meaningful report could be formed.

**V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):**

Claims 1-3, 18-19 comply with PCT Article 33(2) because the prior art, while describing there insulin sensitizer for the treatment of type II diabetes mellitus are silent on the claim recited parameter of a least a threshold plasma concentration level of their inherently effect on bust, and for claim 19, the provision of a delayed pulsed or sustained release composition for it.

Claims 16 and 17 do not comply with PCT Article 33(2) lacking novelty over each of:

Hindley - U.S. 5,002,953

Antonucci - U.S. 5,457,109

Olefsky - U.S. 5,478,852 and U.S. 5,708,012

Regnier - U.S. 5,478,853 and 5,506245

Smithkline Beecham - WO 94/05659 and EP 419035

Encompassed composition of each describing effective amounts of these insulin sensitizer to Type II diabetes mellitus.



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :  A61K 31/44, 31/425		A3	(11) International Publication Number: <b>WO 00/27341</b>
			(43) International Publication Date: 18 May 2000 (18.05.00)
(21) International Application Number: PCT/US99/26746			(81) Designated States: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
(22) International Filing Date: 12 November 1999 (12.11.99)			
(30) Priority Data: 9824893.3 12 November 1998 (12.11.98) GB			
(71) Applicant (for all designated States except US): SMITHKLINE BEECHAM CORPORATION [US/US]; One Franklin Plaza, Philadelphia, PA 19103 (US).			
(72) Inventors; and			
(75) Inventors/Applicants (for US only): BENINCOSA, Lisa [US/US]; 1210 Sugarberry Lane, Collegeville, PA 19426 (US). JUSKO, William [US/US]; 39 Stubwoode Drive, East Amherst, NY 14051 (US).			
(74) Agents: STERCHO, Yuriy, P. et al.; Smithkline Beecham Corporation, Corporate Intellectuel Property, UW2220, 709 Swedeland Road, P.O. Box 1539, King of Prussia, PA 19406-0939 (US).			

(54) Title: NOVEL METHOD OF TREATMENT

## (57) Abstract

A method for the treatment of Type 2 diabetes mellitus and conditions associated with diabetes mellitus, which method comprises the administration to a human or non-human mammal in need thereof, of an effective non-toxic amount of an insulin sensitiser so as to provide a plasma concentration of the insulin sensitiser of at least a threshold level (the "Threshold Plasma Concentration") from within the range of effective plasma levels of the insulin sensitiser, compositions for use in such method and methodology for determining plasma concentrations of active agent use in such methods.

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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DE	Germany	LK	Sri Lanka	SD	Sudan		
DK	Denmark	LR	Liberia	SE	Sweden		
EE	Estonia			SG	Singapore		

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/26746

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :A61K 31/44, 31/425  
US CL :514/275, 252, 369, 337

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/275, 252, 369, 337

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
NONEElectronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
HCAPLUS WPIDS HCAPLUS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -	US 5,002,953 A (HINDLEY) 26 March 1991, (ROSIGLITAZONE).	16, 18-19 -----
Y		1-3, 9, 11-12
X -	US 5,457,109 A (ANTONUCCI et al.) 10 October 1995, CIGLITAZONE, TROGLITAZONE PROGLITAZONE.	16, 18-19 -----
Y		1-3, 9, 11-12
X -	US 5,478,852 A (OLEFSKY et al.) 26 December 1995, (CIGLITAZONE, TROGLITAZONE, ENGLITAZONEP, ROGLITAZONE).	16, 18-19 -----
Y		1-3, 9, 11-12

 Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance		
"E" earlier document published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

08 MARCH 2000

Date of mailing of the international search report

23 MAY 2000

Name and mailing address of the ISA/US  
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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/26746

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,478,853 A (REGNIER et al.) 26 December 1995, (CIGLITAZONE, PROGLITAZONE).	16, 18-19 -----
Y		1-3, 9, 11-12
X	US 5,506,245 A (REGNIER et al) 09 April 1996, (CIGLITAZONE).	16, 18-19 -----
Y		1-3, 9, 11-12
X	US 5,708,012 A (OLEFSKY) 13 January 1998, (ROSIGLITAZONE)	16, 18-19 -----
Y		1-3, 9, 11-12
T,P	US 5,900,435 A (MEGLASSON) 04 May 1999, (PROGLITAZONE).	1-3, 11-12, 16, 18-19
T,P	US 5,902,726 A (KLIEWER et al.) 11 May 1999, (ROSIGITAZONE, PROGLITITAZONE, TROGLITITAZONE, CIGLITAZONE).	1-3, 9, 11-12, 18-19
T,P	US 5,972,973 A (WHITCOMB) 26 October 1999, (TROGLITAZONE-PROGLITAZONE).	1-3, 9, 11-12, 18-19
T,E	US 6,011,049 A (WHITCOMB) 04 January 2000, (ROSIGLATAZONE).	1-3, 9, 11-12, 18-19
X	WO 94/05659 A1 (SMITHKLINE BEECHAM PLC) 17 March 1994, (ROSIGLITAZONE MALEATE).	16, 18-19 -----
Y		1-3, 11-12, 18-19
X	EP 0 4190 35 A1 (SMITHKLINE BEECHAM P.L.C.) 27 March 1994, (ROSIGLITAZONE).	16, 18-19 -----
Y		1-3, 9, 11-12

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US99/26746

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  **Claims Nos.:**  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  **Claims Nos.:**  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  **Claims Nos.: 4-11, 13-15, 17, 20**  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**  

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.